

Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

Claim 1. (Currently Amended): A method for determining ~~the modification~~ conditions ~~for modifying~~ of a therapeutic agent with a biocompatible polymer, to prevent host-mediated inactivation of said therapeutic agent, comprising

(1) assaying the biological activity of a first modified therapeutic agent after said first modified therapeutic agent has been administered to a subject, wherein said first modified therapeutic agent is modified with a biocompatible polymer;

(2) assaying the biological activity of said first modified therapeutic agent after at least one booster dose of said first modified therapeutic agent has been administered to said subject;

(3) carrying out (1) and (2) with a second ~~an additional~~ modified therapeutic agent, wherein said second modified therapeutic agent is modified with a biocompatible polymer and is that has been modified differently from ~~than~~ said first modified therapeutic agent; and

(4) comparing the biological activity of said first modified therapeutic agent with the biological activity of said second ~~additional~~ modified therapeutic agent.

Claim 2. (Currently Amended): The method of claim 1, wherein said second ~~additional~~ modified therapeutic agent is modified with the same biocompatible polymer ~~modifying agent~~ as said first modified therapeutic agent.

Claim 3. (Currently Amended): The method of claim 2, wherein said biocompatible polymer ~~modifying agent~~ is polyethylene glycol (PEG).

Claim 4. (Original): The method of claim 3, wherein said PEG is selected from the group consisting of mono-methoxy succinimidyl butanoate (SBA)-PEG, succinimidyl carbonate (SC)-PEG, aldehyde (ALD)-PEG, and succinimidyl propionate (SPA)-PEG.

Claim 5. (Currently Amended): The method of claim 1, wherein said second additional modified therapeutic agent is modified to the same extent as said first modified therapeutic agent.

Claim 6. (Currently Amended): The method of claim 1, wherein said second additional modified therapeutic agent and said first modified therapeutic agent are modified with different biocompatible polymers ~~modifying agents~~.

Claim 7. (Original): The method of claim 1, wherein said therapeutic agent is a polypeptide.

Claim 8. (Original): The method of claim 7, wherein said polypeptide is used to treat viral infections in patients in need of treatment thereof.

Claim 9. (Original): The method of claim 7, wherein said polypeptide is used to treat cancer in patients in need of treatment thereof.

Claim 10. (Original): The method of claim 7, wherein said polypeptide has a monomeric molecular weight of about 300 daltons to about 300,000 daltons.

Claim 11. (Original): The method of claim 7, wherein said polypeptide is used to lower glutamine levels in a subject.

Claim 12. (Original): The method of claim 7, wherein said polypeptide is used to lower asparagine levels in a subject.

Claim 13. (Original): The method of claim 7, wherein said polypeptide is used to lower asparagine and glutamine levels in a subject.

Claim 14. (Withdrawn): The method of claim 1, wherein said therapeutic agent is a nucleic acid.

Claim 15. (Withdrawn): The method of claim 14, wherein said nucleic acid is used to treat a viral infection in patients in need of treatment thereof.

Claim 16. (Withdrawn): The method of claim 14, wherein said nucleic acid is used to treat cancer in patients in need of treatment thereof.

Claim 17. (Original): A method of preparing a pharmaceutical composition where host-mediated inactivation is prevented, comprising ascertaining the modification conditions of a therapeutic agent by the method of claim 1 and modifying said therapeutic agent according to said modification conditions.

Claim 18. (Original): The method of claim 17, wherein said pharmaceutical composition further comprises an excipient.

Claim 19. (Original): The method of claim 18, wherein said excipient protects said therapeutic agent during lyophilization.

Claim 20. (Original): The method of claim 17, wherein said therapeutic agent comprises glutaminase-asparaginase.

Claim 21. (Original): The method of claim 20, wherein said therapeutic agent is *Pseudomonas* glutaminase-asparaginase.

Claim 22. (Original): The method of claim 21, wherein said *Pseudomonas* glutaminase-asparaginase is modified with polyethylene glycol.

Claim 23. (Withdrawn): The pharmaceutical composition prepared by the method of claim 17, wherein said pharmaceutical composition comprises a glutaminase-asparaginase that has been modified with succinimidyl carbonate polyethylene glycol 5000 (SC-PEG 5000), wherein said glutaminase-asparaginase is modified to an extent of from about 21% to about 49% by SC-PEG 5000, and wherein said composition prevents host-mediated inactivation.

Claim 24. (Withdrawn): The composition of claim 23, wherein said glutaminase-asparaginase is modified from about 26% to about 36% by SC-PEG 5000.

Claim 25. (Withdrawn): The composition of claim 24, wherein said glutaminase-asparaginase is modified about 31% by SC-PEG 5000.

Claim 26. (Withdrawn): The pharmaceutical composition prepared by the method of claim 17, wherein said pharmaceutical composition comprises a glutaminase-asparaginase that has been modified with mono-methoxy succinimidyl butanoate polyethylene glycol 5000 (SBA-PEG 5000), wherein said glutaminase-asparaginase is modified from about 25% to about 58% by SBA-PEG 5000, and wherein said composition prevents host-mediated inactivation.

Claim 27. (Withdrawn): The composition of claim 26, wherein said glutaminase-asparaginase is modified from about 30% to about 40% by SBA-PEG 5000.

Claim 28. (Withdrawn): The composition of claim 27, wherein said glutaminase-asparaginase is modified about 35% by SBA-PEG 5000.

Claim 29. (Withdrawn): The pharmaceutical composition prepared by the method of claim 17, wherein said pharmaceutical composition comprises a glutaminase-asparaginase that has been modified with aldehyde polyethylene glycol 2000 (ALD-PEG 2000), wherein said glutaminase-asparaginase is modified from about 45% to about 65% by ALD-PEG 2000, and wherein said composition prevents host-mediated inactivation.

Claim 30. (Withdrawn): The pharmaceutical composition prepared by the method of claim 17, wherein said pharmaceutical composition comprises a glutaminase-asparaginase that has been modified with succinimidyl propionate polyethylene glycol 5000 (SPA-PEG 5000), wherein said modified glutaminase-asparaginase is modified from about 25% to about 65% by SPA-PEG 5000, and wherein said composition prevents host-mediated inactivation.

Claim 31. (Withdrawn): The composition of claim 30, wherein said glutaminase-asparaginase is modified from about 40% to about 55% by SPA-PEG 5000.

Claim 32. (Withdrawn): A composition comprising a glutaminase-asparaginase, wherein said glutaminase-asparaginase has been modified with succinimidyl carbonate polyethylene glycol 5000 (SC-PEG 5000) to an extent of about between 21% and 49%.

Claim 33. (Withdrawn): The modified therapeutic composition of claim 32, wherein said glutaminase-asparaginase has been modified to an extent of about between 26% and 36%.

Claim 34. (Withdrawn): The modified therapeutic composition of claim 33, wherein said glutaminase-asparaginase has been modified to an extent of about 31%.

Claim 35. (Withdrawn): A composition comprising a glutaminase-asparaginase, wherein said glutaminase-asparaginase has been modified with succinimidyl butanoate polyethylene glycol 5000 (SBA-PEG 5000) to an extent of about between 25% and 58%.

Claim 36. (Withdrawn): The modified therapeutic composition of claim 35, wherein said glutaminase-asparaginase has been modified to an extent of about 30% to 40%.

Claim 37. (Withdrawn): The modified therapeutic composition of claim 36, wherein said glutaminase-asparaginase has been modified to an extent of about 35%.

Claim 38. (Withdrawn): A composition comprising a glutaminase-asparaginase, wherein said glutaminase-asparaginase has been modified with aldehyde polyethylene glycol 2000 (ALD-PEG 2000) to an extent of about between 45% and 65%.

Claim 39. (Withdrawn): A composition comprising a glutaminase-asparaginase, wherein said glutaminase-asparaginase has been modified with succinimidyl propionate polyethylene glycol 5000 (SPA-PEG 5000) to an extent of about between 25% and 65%.

Claim 40. (Withdrawn): The modified therapeutic composition of claim 39, wherein said glutaminase-asparaginase has been modified to an extent of about 40% to 55%.